

关注电子烟独有的毒性特征

Silke Schmidt

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许多家长和儿科医生担忧电子烟对于青少年的诱惑，他们并不是唯一担心电子烟危害的人群。2017年3月，一名高中三年级学生联系了Terry Gordon，询问有关科学展览会的想法。在交谈中，这个男孩提到了他对同学在学校洗手间里吸电子烟的担忧。

“[这使我]突然萌生了一个想法，”纽约大学格罗斯曼医学院（Grossman School of medicine）的环境医学教授Gordon回忆道。“我们决定进行一些空气测量，看看电子烟是否对那些不吸烟的孩子有害。”

在校方、教师、教育委员会以及家长教师协会的支持下，Gordon的团队最终在一所高中和一所初中的洗手间安装了空气监测器。研究人员在这些洗手间测量到与电子烟相关的尼古丁水平与居民吸烟严重的纽约市公共住房的水平相似，Gordon说道。¹

对于电子烟是否与尼古丁替代疗法一样有效或更有效地帮助戒烟，目前还没有定论。²迄今为止，美国食品药品监管局（FDA）还没有批准电子烟作为戒烟的辅助工具。³

尽管电子烟可能不会使使用者暴露于烟草燃烧产生的所有有毒物质，但与电子烟气溶胶暴露相关的健康风险的表征尚未明确。⁴这意味着，吸烟者改用电子烟后减少的危害应该与非吸烟者面临的潜在风险进行权衡，这些非吸烟者认为电子烟比香烟更具吸引力，而且认为它比香烟更安全。

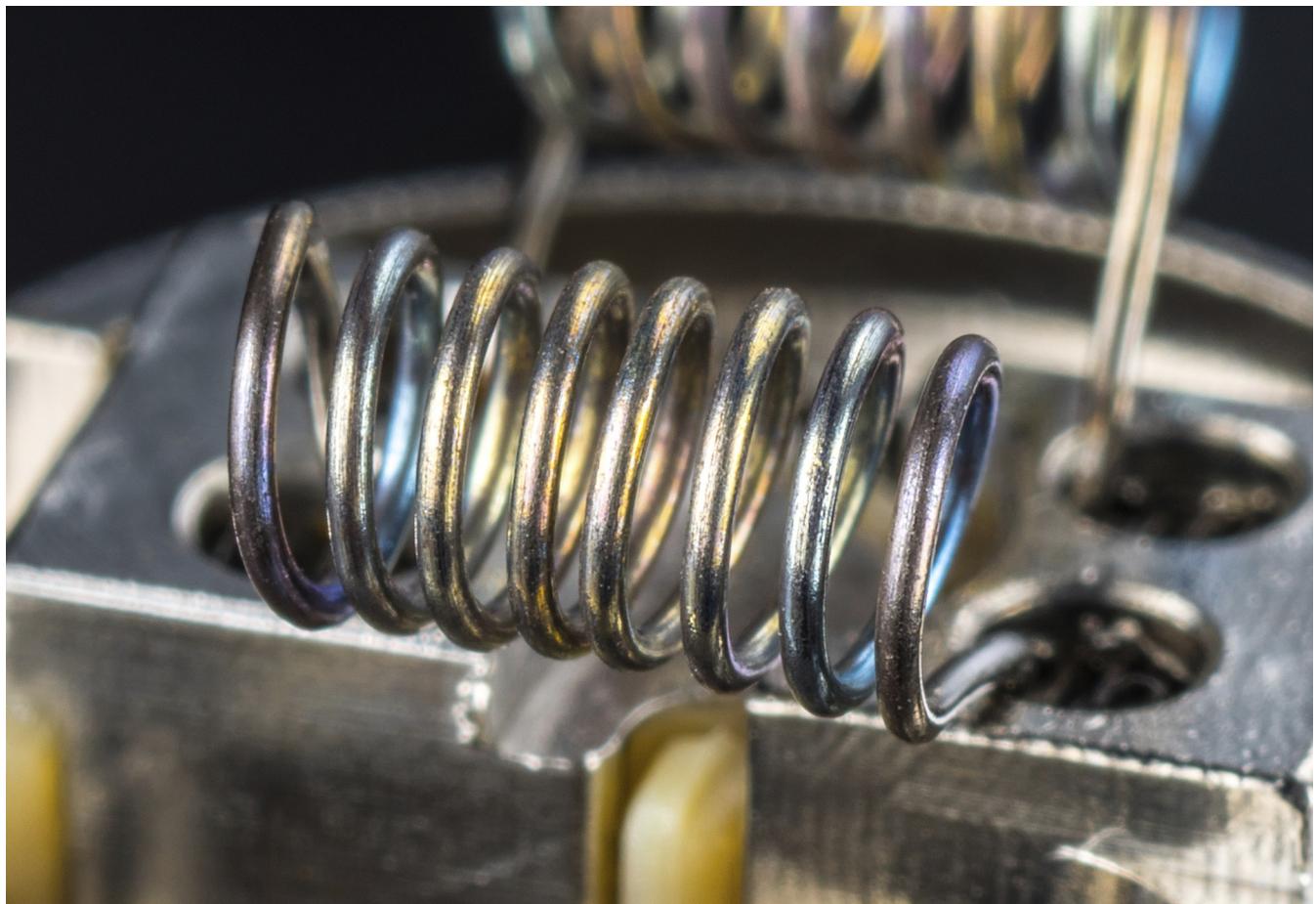
2019年美国爆发的“使用电子烟或电子雾化产品造成肺损伤”（e-cigarette, or vaping, product use associated lung injury, EVALI）影响了许多年轻人；超过一半的人年龄在25岁以下。⁵尽管这很可能是由添加了维生素E醋酸盐的含有四氢大麻酚（THC）的电子烟引起的，⁵但这一事件加剧了公众对同时发生的青少年电子烟流行的担忧，且越来越多的科学证据支持了这一观点，电子烟远非安全。⁶

可燃香烟与电子烟

电子烟含有电池供电的加热元件，通常是一个金属线圈，它可以加热一种混合了溶剂、尼古丁和调味化学品的“电子液体”。使用者将电子液产生的气溶胶吸入肺部。制造



近期报告高中生使用电子烟的比例从2011年的1.5%上升到2019年的27.5%。²⁶青少年使用电子烟的比例迅速增长是FDA打击以青少年消费者为目标市场的制造商的原因之一。Image: CC BY 4.0 (cropped original).



全新的加热线圈比旧的释放出更多的金属粒子。但这只是单个设备（电子烟）影响金属总排放量的其中一个特征。Image: © iStockphoto/gawriloff.

商不需要公开电子液体中的成分（尽管他们必须向 FDA 报告），而且很多品牌标签上和实际尼古丁含量之间存在很大的差异。^{7,8,9,10}

2006 年电子烟进入美国市场。¹¹ 随着时间的推移，其设计发生了很大的变化。第一代“仿真烟”类似于真正的香烟；第二代笔状电子烟配有可充电电池和可填充暗盒；第三代“mods”有更大的容量，有可变电压设置和其他可调功能；体积更小的第四代电子烟（包括 JUUL[®]）配备了一次性或可再填充暗盒，但手动调节的设置很少（如果有的话）。¹¹

然而，尽管这个市场复杂多样，但原理很简单。“电子烟不过就是一个化学反应堆。”弗吉尼亚联邦大学（Virginia Commonwealth University）健康心理学教授 Thomas Eissenberg 说道。电子烟的功率（以瓦特为单位）是电池电压和线圈电阻的相互作用。许多电子烟的功率在 5 到 10 W 之间，最高可达 200 W。¹² 据 Eissenberg 介绍，电子烟的功率可能对使用者暴露于尼古丁和其他有毒物质的影响最大。“你投入到反应堆的能量越多，电子液体成分热降解成有害化学物质的可能性就越大。”他说道。

由于大功率的电子烟每口抽吸时能雾化更多的液体，^{13,14,15} 因此抽吸电子烟时血浆中的尼古丁含量会迅速上升。一些研究表明，一支电子烟所释放的尼古丁量与一支可燃香烟相等，在某些情况下甚至更高。^{16,17} 此外，一些品牌

（最著名的 JUUL[®]）在他们的电子液体中使用口感柔和的质子化尼古丁（“尼古丁盐”）。¹⁸ 将尼古丁与弱酸结合会产生尼古丁盐，这比苦味的无碱（未质子化的）尼古丁能形成更美味的烟雾。¹⁹ 也有证据表明，尼古丁盐配方与尼古丁产量或暴露量的增加，^{19,20} 以及尼古丁快速吸收相关。²¹

在过去几十年里，美国吸烟人数的下降很大程度上归因于烟草控制措施，如香烟税、禁烟令以及健康教育运动。²² 在美国，20 世纪 60 年代超过 55% 的男性和 35% 的女性吸烟，而在 2018 年只有 13.7% 的成年人吸烟。²³ 全球范围内，以年龄标准化计算 2015 年每日吸烟率估计男性为 25.0%，女性为 5.4%。²⁴ 大多数男性吸烟率明显超过全球平均水平的国家在中欧、东欧、中国以及东南亚。而西欧和中欧女性的吸烟率高于全球平均水平。²⁴

自 2011 年以来，美国高中生的吸烟率有所下降。²⁵ 与此同时，最近报告使用电子烟的高中生比例从 2011 年的 1.5% 上升到 2019 年的 27.5%。²⁶ 此外，有 10.5% 的初中生称他们目前有吸电子烟，这使得电子烟成为美国青少年中最受欢迎的尼古丁享用装置。²⁶ 尽管 2018 年只有 3.2% 的成年人表示他们偶尔或每天吸电子烟，²³ 但也有报告显示，成年人电子烟的使用呈上升趋势。²⁷

2015 年推出的 JUUL[®] 电子烟，其受欢迎程度尤其显著。到 2019 年，分别有 59% 和 54% 的美国高中和初中电子



制造商和电子烟使用者，用 PG 和 VG（也称为植物甘油或甘油）按不同比例调制溶剂，从电子液中获得理想效果。这些包括口味的强度、“喉咙冲击”的强度（或吸入尼古丁的感觉），以及由此产生的烟云大小。¹¹² Image: CC0 Public Domain.

烟用户选择 JUUL® 作为他们的常用品牌。²⁶ 其时尚和易于隐藏的设计，¹⁸ 以及其吸引人口味的针对性营销策略（最近受到监管部门审查²⁸），使该品牌深受青少年的欢迎。^{18,29}

调查显示，可选择不同的口味是电子烟对这个年龄段最吸引人的特点之一。³⁰ 其结果是，青少年时期吸电子烟会增加他们在日后吸烟的可能性，无论是否同时使用电子烟。^{31,32,33} 一项综述研究发现，美国和其他几个国家的青少年、男性和白色人种比其他群体更有可能消费电子烟。³⁴ 与香烟相比，电子烟具有金属、溶剂和调味化学品独特的毒性。³⁵ 这3类均被报告有危害健康的证据。

电子烟中的金属

约翰·霍普金斯大学环境健康与工程助理教授 Ana María Rule 从 2014 年开始测量电子烟中的金属含量。她最先开始研究电子液体，其次是气溶胶和使用者样本，包括尿液、唾液和呼出的冷凝物。

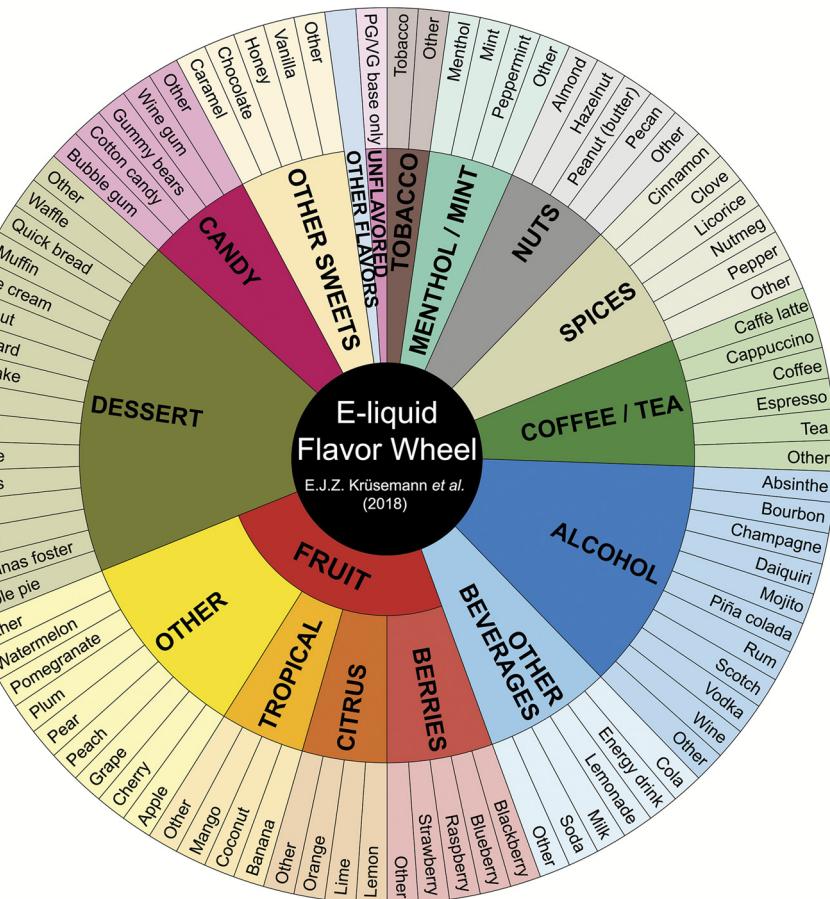
她的研究和其他研究表明，镍和铬是对电子烟使用者关系重大的金属暴露物。^{36,37,38,39,40,41,42,43} 使用者尿液和唾液样本中的镍和唾液样本中的铬与电子烟气溶胶中的金属浓度密切相关。⁴⁴ 尽管这类暴露对人类健康的影响只能在长期研究中确定，但六价铬和一些镍化合物是已知的肺癌致癌物。^{45,46}

在电子烟气溶胶中也检测到了其他金属，尽管它们的含量比镍和铬变化更大。它们包括铜、锌、锰、砷等。³⁵ 金属来源可能是线圈，特别是镍和铬、焊接和接线，以及电子烟主体。^{42,47} 烟叶也含有多种不同浓度的重金属。^{48,49} 然而，电子烟制造商声称，他们使用的是高度纯化的药物级尼古丁电子液，³⁵ 而烟叶可能只用于烟草调味产品。

每个电子烟的特征可以影响使用者吸入的金属量。⁴² “我们预计旧线圈会释放出更多的金属，但实际上却恰恰相反，” Rule 说道。“全新的线圈释放的金属最多。” 她解释说，线圈每次加热都会退化一点。随着时间的推移，热量分解了最初用来制造线圈的原始金属合金。Rule 还发现，由于氧化残留物的堆积降低了线圈的加热效率，用户往往会频繁更换线圈。这意味着需要更多次吸入来摄入等量的尼古丁。

金属排放也可能受到电子烟瓦特数的影响。一项研究表明，一些金属的气溶胶浓度随瓦特数的增加而升高，但在某一点后趋于稳定甚至下降。⁴² 目前正在研究电子液 pH 值的显著变化是否会影响金属排放，^{50,51} Rule 说道。

她还指出了其他潜在的相互作用。“常见的调味化学品的吸入可能有助于把金属带入大脑和心脏组织细胞，”她说。例如麦芽酚，电子烟中一种常见的调味化学品，非常容易与铁结合。⁵² “我认为这是一个迫切需要更多研究的领域，” Rule 说道。



有关使用者的电子烟偏好和习惯的研究表明，他们在描述口味方面缺乏一致性。2018年，研究人员开发了一个“口味转盘”，由13个主要类别和90个子类别组成。¹¹³通用的口味分类词可以更容易地比较跨研究的结果。Image: © The Authors 2018. Published by Oxford University Press on behalf of the Society for Research on Nicotine and Tobacco. Originally published in Krüsemann EJZ, Boesveldt S, de Graaf K, Talhout R. 2019. An e-liquid flavor wheel: a shared vocabulary based on systematically reviewing e-liquid flavor classifications in literature. Nicotine Tob Res 21(10):1310–1319, DOI: 10.1093/ntr/nty101.

电子液中的溶剂

电子液中的溶剂通常是丙二醇（propylene glycol, PG）和植物甘油（vegetable glycerol, VG）按不同比例混合而成的。¹⁰ 研究人员已对这些溶剂的吸入毒性产生担忧，即使没有尼古丁和调味化学品。³⁵

当PG和VG受热时，分解产物包括3种醛类：甲醛、丙烯醛和乙醛。^{53,54}作为羰基化合物的主要部分，这些有毒物质也存在于烟草烟雾中。一些电子烟气溶胶含有甲醛半缩醛（formaldehyde hemiacetals），这是最近发现的一种甲醛形式，它可能比气态甲醛更易深入地沉积在肺部。^{53,55}

当前市场上的溶剂混合物的比例有100%的PG、PG和VG各占50%，以及100%的VG。¹⁰研究表明，VG含量较高的电子液比PG含量较高的电子液产生更多的甲醛和丙烯醛，特别是在大功率条件下。这可能会使电子烟使用者比吸烟者暴露于更高的醛水平下，^{10,56,57,58}而且这对“腾云驾雾者”来说是令人担忧的，他们更喜欢含有大量VG的电子液，因为它们会产生更大、更明显的烟云。¹⁰另一方面，研究表明，较高的PG含量会增强尼古丁向血液中释放，可能会加快成瘾发展的速度。⁵⁹

在对溶剂的详细分析中，研究人员对几组小鼠进行了为期4个月的实验，分别将它们置于以下4种暴露类别：⁶⁰

PG/40 VG 比例混合物中的气溶胶，含或不含尼古丁；香烟烟雾；或室内空气。⁶⁰与烟雾暴露的动物不同，气溶胶暴露的小鼠没有出现肺部炎症或肺气肿。然而，它们确实出现了肺上皮细胞和常驻免疫细胞的变化，使它们比呼吸室内空气的小鼠更容易感染流感。

PG和VG添加剂是公认的安全的食品乳化剂。^{61,62}它们也用于化妆品。然而，当吸入时它们的乳化特性似乎促进了肺细胞中不同脂质的聚积，而这一特征并没有在烟草烟雾暴露组的小鼠中观察到。⁶⁰这项研究的发现是全新的，但与先前报道的仅暴露于溶剂气溶胶中的人类肺组织的变化一致。^{63,64}作者总结道，他们的发现“拉响了对[电子烟]可能对肺泡产生的潜在有害影响的警报”，⁶⁰并呼吁对吸入溶剂进行进一步的毒性研究。

调味化学品与溶剂的相互作用

荷兰比尔特霍芬（Bilthoven）国家公共健康与环境研究所（National Institute for Public Health and the Environment）化学家、资深科学家 Reinskje Talhout 认为，调味电子烟最主要的问题是它们掩盖了尼古丁的味道。“这使得产品对新用户更有吸引力，” Talhout 说道。



新的证据表明，二手暴露于电子烟气溶胶可能会使旁观者暴露于潜在的有害化学物质。截至 2020 年 1 月 2 日，美国 22 个州和地区已经限制在无烟环境下使用电子烟。¹¹⁴ Image: © iStockphoto/mediaphotos.

另一个问题是口味背后的化学成分。在美国⁶⁵ 和欧洲⁶⁶ 市场中，这几百种不同化学物质的组合产生了数千种口味，Talhout 说道。此外，Ilona Jaspers 指出，在复杂的电子液环境中，混合这些化学物质可能产生二级和三级反应产物。Jaspers 是北卡罗莱纳大学教堂山分校（University of North Carolina at Chapel Hill）微生物和免疫学系以及北卡罗莱纳大学医学院（UNC School of Medicine）儿科系的教授。

与溶剂类似，在早期电子烟研究之前，食品和化妆品中的调味化学品可能普遍被认为安全，故没有经过吸入毒性测试。^{67,68,69} 当 Jaspers 和其他研究人员^{67,68,69} 意识到青少年使用电子烟的增长趋势后，他们开始研究人体细胞中的调味化学品。

对于 Jaspers 来说，肉桂醛（cinnamaldehyde）是第一个突出的化合物。它是几种流行口味中常见的成分，对直接暴露在电子液中的人类肺细胞显示出强烈的细胞毒性作用。⁷⁰ “最初我们很惊讶，” Jaspers 回忆道。“但作为一种芳香 α,β -不饱和醛类，又非常合理，因为这是一个非常非常活跃、对健康有很大影响的化学物质。” 其他已知的 α,β -不饱和醛类具有显著的化学反应性，包括丙烯醛，她说道。

肉桂醛的发现^{70,71,72} 促使了对芳香醛同一功能类别的其他化学物质的体外（*in vitro*）试验。乙基香兰素（香草口味）和苯甲醛（杏仁和樱桃口味）也有类似的效果。^{73,74}

Jaspers 实验室使用的人体细胞调味化学品的最强暴露量比电子液体和气溶胶报告的范围还低了 2 个数量级。⁷³ 一些调味化学品从电子液体高效转移到气溶胶中，其中一些电子烟报告的平均转化率高达 86%。⁷⁵ 然而，电子烟使用者生物样本中这些化学物质的含量目前还不清楚。⁷³

研究人员还发现芳香醛和溶剂之间的反应在室温下就可能发生，例如，当电子烟放在商店货架上时。在一些体外（*in vitro*）试验中，反应产物比单独调味剂更具危害性。^{76,77} 例如，苯甲醛 PG 缩醛（也称乙缩醛）比苯甲醛对人体细胞的毒性更大，⁷⁴ 而 JUUL® 的焦糖奶油（Creme Brulee）电子液中的调味剂与 PG 和 VG 形成了强效缩醛。⁷⁸ Jaspers 指出，缩醛只是许多可能的化学相互作用中的一种。

其他具有细胞毒性的化学物质包括麦芽酚和乙基麦芽酚；后者存在于 80% 的评估产品中。^{79,80} 特别值得关注的是黄油味双乙酰，它是酮类家族的一员。尽管吸入时安全，但雾化的双乙酰会导致某些行业员工患上闭塞性细支气管炎（“爆米花肺”）和其他严重呼吸道疾病。^{81,82} 调查人员最近报告的证据表明，电子烟可能导致了一名加拿大青少年患上闭塞性细支气管炎。⁸³

继之前的一份报告之后，⁸⁴ 研究人员在 51 种电子液产品中发现有 39 种的双乙酰含量超过检测限，其中包括那些研究人员认为可能特别吸引年轻人的名字和口味的产品。^{85,86} 此



电子烟长期以来一直被吹捧为吸烟的健康替代品。电子烟使用者确实可以避免许多与吸烟有关的毒性暴露。然而，电子烟本身也有潜在的有害暴露。Image: © Philip Brookes/Alamy Stock Photo.

外，随着时间的推移，尼古丁可能会加速乙偶姻（acetoin，酮类家族中另一种常见的调味化学品）向双乙酰的转变。⁸⁷

Jaspers 指出，金属是一种化学催化剂，可以进一步增强电子液成分的反应活性。此外，她说道，一些调味化学品可能会干扰尼古丁的新陈代谢和解毒能力，并增强其稳定性。

电子烟使用者和旁观者的潜在健康影响

一个多世纪以来人们一直在研究香烟烟雾，它含有 7000 多种化学物质，其中至少 250 种是有害的，69 种是已知的致癌物质。⁸⁸ 估计有 85% 的肺癌和 50% 的膀胱癌是由吸烟引起的。⁸⁹

鉴于电子烟进入市场的时间比较短，它们的长期健康影响尚不确定。的确，与吸烟者相比，电子烟使用者体内的某些化学物质，如烟草特有的亚硝胺（tobacco-specific nitrosamines, TSNAs）和多环芳烃的含量要低得多。⁹⁰ “仅使用电子烟的人不会死于（与吸烟有关的）肺癌，” Eissenberg 说道。“但是，他们可能死于其他癌症或其他疾病的几率，在使用电子烟几十年后，是否会高于不吸电子烟或吸烟的人，我们还不得而知。”

流行病学和实验证据表明，电子烟气溶胶对肺、心血管、免疫系统、^{4,35,91,92,93} 大脑^{94,95} 以及口腔⁹⁶ 存在有害影响。在小鼠中发现患肺癌和膀胱尿路上皮癌的风险增加。⁹⁷

Talhout 和其他人在有限样本的研究条件下发现了二手暴露有害化学物质的证据，比如金属和 TSNAs。^{98,99,100} “这是一个重要的信息，旁观者[可能]会受到电子烟的伤害，” Talhout 说道。“我认为禁止在公共场所使用这些产品是有道理的。”

纽约大学的 Gordon 正在指导一项进行中的小组研究，研究对象是至少有一个吸烟、吸电子烟或使用水烟管的成年人，以及一个成年人或儿童不吸烟的家庭。¹⁰¹ “我们用快速、无创的方法测量家庭空气质量和心肺功能，并观察电子烟气溶胶的二手暴露对健康的影响。”他说道。

电子烟的法规

包括巴西、印度和乌拉圭在内的一些国家已经禁止销售所有电子烟或含有释放尼古丁的产品。^{102,103,104} 欧盟已对电子液体中的尼古丁设定了 20 mg/mL 的监管限值，以防止电子烟释放的尼古丁超过标准香烟剂量。¹⁰⁵

在美国，电子烟和其他称为电子尼古丁释放系统（electronic nicotine delivery systems, ENDS）属于《烟草控制法案》（Tobacco Control Act）的范畴。2016 年 8 月 8 日生效的“认定规则”中 FDA 做出了这一决定（这意味着 ENDS 被认定受该法案的约束）。¹⁰⁶ 当时市场上的所有品牌的电子烟都必须在上市前获得 FDA 的批准；然而，没有一家制造商遵守这个规定。换句话说，当时出售的所有 ENDS 产品

都应被视为非法销售。¹⁰⁷（本文撰写时，市场上仍然没有ENDS产品得到FDA的实际批准。）

起初，FDA向制造商发出了警告信，但没有进一步的行动。随着年轻人吸电子烟率开始飙升，情况发生了变化。2020年1月，FDA宣布开始执行该法案。¹⁰⁷由于市场上没有一种电子液体符合规定，公司被允许有一个月的时间将产品下架。如果制造商希望恢复销售，必须在2020年5月12日前向FDA提交上市前烟草产品申请。¹⁰⁶这些申请必须提供“可以证明产品适合保护公众健康的科学数据”。¹⁰⁸

总的来说，电子烟的监管行动是复杂的，需要在保护非吸烟者免受伤害和减少现有吸烟者的伤害之间取得平衡。“完全[改用电子烟]的吸烟者暴露在较低水平的[某些]致癌物和其他有毒物质中。”^{90,109}加州大学旧金山分校医学助理教授Gideon St.Helen说道。“这降低了一些与烟草有关疾病的风险，并可能对公众健康有益。”

其他专家同意这一考量，尽管电子烟对公共健康的净影响长期取决于人口统计数据和未来的人口增长。⁴例如，当出生率不断增长时可能会优先考虑降低青少年的风险，这与终生吸烟的老年人比例不断增长时的考虑可能有所不同。

其他一些可能的政策，比如只允许希望戒烟的吸烟者以处方方式购买电子烟，也受到了批评。“有些人认为，以处方为基础的市场对吸烟者是不公平的，因为它为获得更安全的产品设置了障碍，”约翰·霍普金斯大学疾病预防教授Joanna Cohen说道，她的学术领域是从全球角度研究烟草控制。“综合戒烟系统最好的例子是英国，英国的公共健康专家长期以来一直认为，吸烟有害健康，其他任何比吸烟好的东西都应该易于获得。”

对St.Helen来说，这是一个合理的论点。“我们已经知道，在美国，少数族裔和弱势群体更难获得尼古丁替代疗法，”他说道。“我们不希望电子烟也发生同样的问题。但是以某种方式让电子烟只对吸烟的成年人开放，这会是一件好事。”

Talhout和Jaspers呼吁制定检验调味化学品和溶剂吸入毒性的政策指南。Eissenberg建议将欧盟的尼古丁上限与他合作开发的尼古丁通量数学模型结合起来。^{110,111}“由于解决电子烟中多种设计成分非常困难，监管应该把重点放在最终结果，”他说道。Eissenberg的团队表明，该模型预测的尼古丁通量（电子烟释放尼古丁的速率）与实际测量高度相关，主要取决于电子烟功率和电子液尼古丁含量。¹⁵

尼古丁通量政策将确保使用者不能规避大功率电子烟的电子液中的尼古丁上限。它将适用于含有尼古丁盐或游离尼古丁（free-base nicotine也称作自由基尼古丁）的配方。但它只适用于“封闭系统”的电子烟，这些电子烟的组件无法更换或重新填充，Eissenberg说道。目前美国市场对开放系统电子烟的监管更具挑战性，他补充道。

其他一些紧急行动项目不只局限于法规。“我们需要帮助那些从吸电子烟开始就对尼古丁上瘾的孩子，”Jaspers说道。“这需要科学家、家长和医务人员联合起来开发新的工具，让他们摆脱这个危险的习惯。教师将有助于普及有关电子烟潜在危害的教育。”

Silke Schmidt，博士，居住在威斯康辛州麦迪逊市，撰写关于科学、健康和环境的文章。

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